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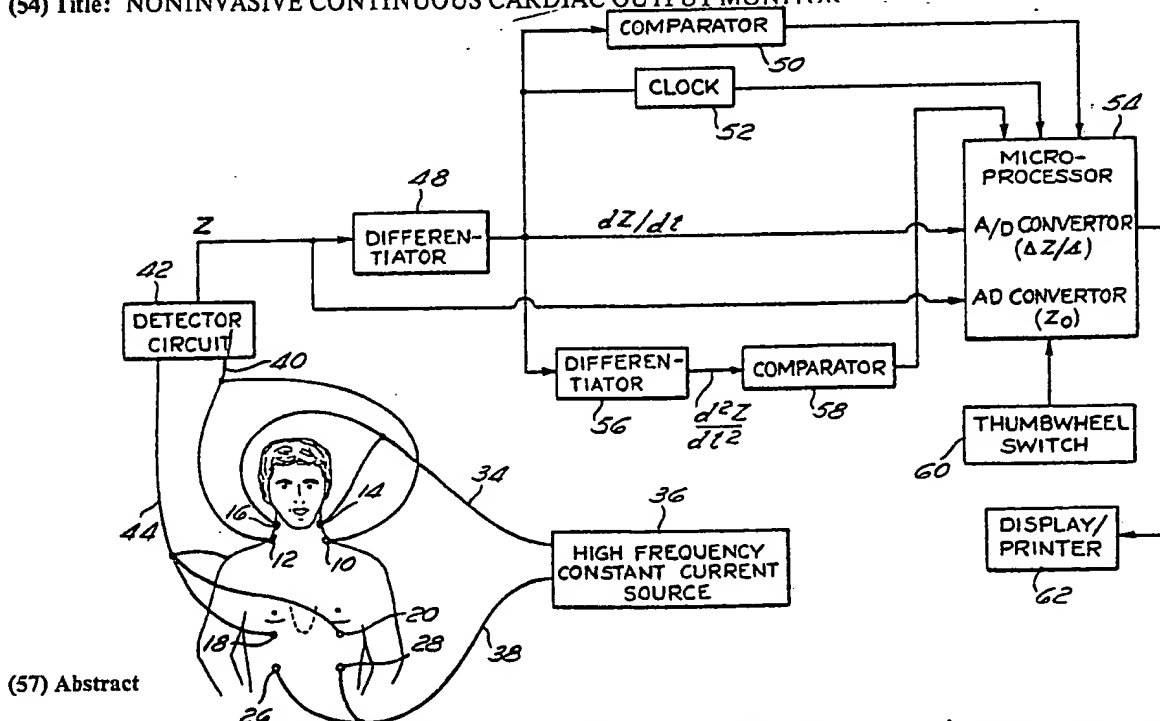
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(54) Title: **NONINVASIVE CONTINUOUS CARDIAC OUTPUT MONITOR**

Apparatus and methods for using the electrical bioimpedance measurements to monitor parameters associated with blood flow in a segment of body tissue. The invention eliminates the effect of respiration from the thoracic impedance as a function of time to provide a signal indicative of pulsatile thoracic impedance changes continuously. The pulsatile thoracic impedance signal is processed to produce signals indicative of the ventricular ejection time and the maximum rate of change of pulsatile thoracic impedance which are used in a microprocessor (54) to calculate the volume of the blood pumped per stroke according to an improved systolic upstroke equation.

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NONINVASIVE CONTINUOUS CARDIAC OUTPUT MONITOR

Background of the Invention

This invention is generally related to apparatus and methods for measuring parameters associated with the flow of blood through a body segment. More particularly, this invention is related to apparatus and methods for monitoring cardiac output. Still more particularly, this invention is related to noninvasive apparatus and methods for continuously monitoring cardiac parameters.

Cardiac output is the volume of blood which the heart pumps in one minute and is one of the most important cardiovascular parameters. The cardiac output reflects the supply of oxygen and nutrients to tissue. Measurements of cardiac output provide invaluable clinical information for quantifying the extent of cardiac dysfunction, indicating the optimal course of therapy, managing patient progress, and establishing check points for rehabilitation in a patient with a damaged or diseased heart, or one in whom fluid status control is essential. Exercise as well as pathological conditions of the heart and circulatory system will alter cardiac output; therefore, the measurement of cardiac output is useful both in rehabilitation and in critically ill patients.

Instrumentation currently in use for invasive and noninvasive measurement of cardiac output has several disadvantages. Cardiac output may be measured either invasively or noninvasively. The invasive techniques for measuring cardiac output involve penetration of the skin by a catheter, require complex instrumentation which must be operated by skilled personnel, and present a risk to the patient. Invasive techniques such as indicator dilution and thermal dilution allow only intermittent measurement of cardiac output since it is possible to obtain only one determination of cardiac output per injection in dilution methods.



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5 The noninvasive techniques for measuring cardiac
parameters include ballistocardiography, electrical
impedance measurements, ultrasonics, phonocardiography and
vibrocardiography. The instrumentation involved in
present noninvasive techniques for measuring cardiac
output is complex, expensive, inconvenient to use and
requires highly trained operators. Existing electrical
impedance instrumentation permits determination of cardiac
output only during voluntary apnea, which means that the
10 patient must hold his breath. Therefore, existing
electrical impedance instrumentation is unsuitable for use
with critically ill or unconscious patients.

Electrical bioimpedance measurements permit
quantification of blood flow as a result of changes in
electrical conductivity of a body segment. The electrical
15 impedance technique for measuring cardiac output is based
upon changes in thoracic electrical impedance caused by
cardiovascular activity. The change in impedance has
several origins:

20 1. Cardiovascular activity causes pulsatile
impedance changes. Approximately one-half of the
pulsatile impedance change is related to volumetric
changes of blood in the arteries as a result of arterial
pressure compliance because blood is the most electrically
25 conductive substance in the body. The other half of the
pulsatile impedance change is caused by variation of the
specific resistivity of blood as a function of blood
velocity, which is related to the alignment of red blood
cells.

30 2. Ventilation causes pulsatile impedance changes.
In the thoracic region, the ventilation related impedance
changes are directly proportional to the varying amount of
air in the lungs while in the extremities the ventilation
related impedance changes are caused by variation of the
35 venous pool as a result of ventilation.



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3. Edema and blood pooling cause nonpulsatile impedance changes.

The impedance changes listed as (1) above enter into the calculation for quantification of cardiac output. The ventilation impedance changes (2) represent an unwanted background signal which must be suppressed to obtain accurate results.

The electrical impedance technique for measuring cardiac output has a significant advantage over the dilution methods, in addition to being noninvasive, in that the result of the measurement of the impedance change is the stroke volume, which is the volume of blood pumped per one heart contraction, which, when multiplied by heart rate, results in cardiac output. Therefore, stroke volume provides the clinician with beat-two-beat information on cardiac function. Indicator dilution methods determine average cardiac output only. However, the electrical impedance measurement technique has failed to gain wide acceptance since it has demonstrated a good correlation with invasive techniques only on healthy individuals. A strong deviation from expected values of cardiac output occurred in patients with pulmonary apnea or increased thoracic fluid content. The deviation is related to the mathematical structure of the equations used to calculate the stroke volume.

The first useful equation to quantify stroke volume from the cardiovascular impedance change was described by Nyboer, electrical impedance plethysmography, Charles C. Thomas, 1959. Nyboer's equation is:

$$SV = \frac{RL^2}{Z_0^2} Z$$

which uses the systolic downstroke extrapolation method on a graph of the thoracic impedance as a function of time to determine the cardiovascular impedance change during a heartbeat. R is the resistivity of blood of the subject,



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L is the average distance between sensing electrodes attached to the subject, ΔZ is the cardiovascular impedance change, and Z_0 is the base electrical impedance of the thorax. Typical magnitudes of the thoracic variables for a healthy subject are $Z_0 = 30$ ohms, $R = 150$ ohm centimeters, $L = 30$ centimeters, and $\Delta Z = 30$ milliohms. Since ventilation impedance changes are typically an order of magnitude larger than the cardiovascular impedance changes, all measurements using Nyboer's method have to be performed during voluntary apnea. Therefore, Nyboer's method is currently used in peripheral applications only.

Kubicek et al, "The Minnesota Impedence Cardiography-Theory and Applicatons", Biochem. Eng. 9: 410, 1974, describe an improved equation for the calculation of stroke volume. Kubicek introduced the product of two cardiovascular variables, ventricular ejection time T and the maximum rate of impedance change $\Delta Z/\text{sec}$, in place of a single cardiovascular variable, ΔZ used in Nyboer's equation. The maximum rate of impedance change can be derived either from the graphical extrapolation of systolic upstroke impedance change to maintain a rate of impedance change in one second or from the maximum value of electronically derived first derivative of impedance change. Kubicek's equation is:

$$SV = \frac{RL^2}{Z_0^2} T (\Delta Z/\text{sec})$$

where SV = stroke volume, R is the specific resistivity of blood, L is the distance between sensing electrodes, Z_0 is the base electrical impedance, T is the ventricular ejection time, and $\Delta Z/\text{sec}$ is the maximum rate of impedance change.

In spite of the clear advantage of being capable of noninvasive cardiac output determination, electrical bioimpedance measurements have not gained wide spread use



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in thoracic measurements for the following reasons:

1. Good correlation against other techniques could be demonstrated only on healthy individuals;

2. Calculated cardiac output of patients with increased thoracic fluid content was much higher than the expected value;

3. There are unresolved questions about the influence of hematocrit on the accuracy of calculation of cardiac output;

4. The determination of cardiac output could be performed only intermittently with the subject in voluntary apnea;

5. The electrodes used with prior art devices are not suitable for long term monitoring; and

6. The existing instrumentation is high in cost and very complex, requiring skilled operators.

Therefore, there is a need for a system for monitoring cardiac output parameters which may be used continuously, is simple to operate, is safe for both the subject and operators, has the versatility to measure and display several cardiovascular variables for every heartbeat and which has relatively low initial cost and low operating costs.

Summary of the Invention

The present invention overcomes the deficiencies associated with prior art devices and methods for using bioimpedance measurements to monitor cardiac output parameters. The invention provides a noninvasive apparatus and method using the principle of electrical bioimpedance to continuously monitor cardiac output. A small, constant amplitude, high-frequency electrical current flowing parallel to the spine develops a voltage across the thorax. The voltage across the thorax is proportional to the thoracic electrical impedance. The dimensions of the thorax, thoracic electrical impedance, ventricular ejection time, and the maximum rate of



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impedance change are parameters used in an improved systolic upstroke equation to calculate the stroke volume. Cardiac output is obtained by multiplying the stroke volume by the heart rate.

5 The invention utilizes pregelled spot electrodes to facilitate continuous monitoring of cardiac output. The invention is simple to operate in that the operator needs only to attach the electrodes to the patient, turn the power on, enter the thoracic dimensions into the system, and select the desired variable to be displayed and
10 monitored.

Cardiac output parameters are monitored by producing an electrical signal indicative of the thoracic impedance as a function of time and eliminating the effects of respiration from the thoracic impedance signal to produce
15 a pulsatile impedance signal indicative of changes in thoracic impedance due to cardiovascular activity as a function of time. By electrically processing the thoracic impedance signal to eliminate the effects of respiration from the signal, the invention overcomes the deficiencies of prior art devices which require measurement of thoracic
20 impedance during voluntary apnea. The electrical signal indicative of the pulsatile thoracic impedance is processed to determine the maximum rate of change of the pulsatile impedance signal. A microprocessor is programmed to use the thoracic base impedance, the ventricular ejection time, the maximum rate of change of pulsatile impedance, and the average distance between
25 upper and lower sensing electrodes to produce signals indicative of stroke volume. The results of calculation can be digitally printed on a printer or may be displayed on a visual display to indicate the base thoracic impedance, the ventricular ejection time, the maximum rate of impedance change, the stroke volume, the heart rate, and
30 the cardiac output.

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Brief Description of the Drawings

Figure 1 illustrates electrode placement to monitor cardiac output of a patient according to the invention;

Figure 2 is a block diagram of the electrical circuitry of the invention;

Figure 3 is a graph of thoracic impedance as a function of time during normal respiration;

Figure 4A is a graph representing an electrocardiogram signal;

Figure 4B is a graph of changes in thoracic impedance due to cardiovascular activity as a function of time;

Figure 4C is a graph of the first derivative of the graph of Figure 4B;

Figure 4D is a digital representation of the graph of Figure 4C;

Figure 4E is a graph of the second derivative of the graph of Figure 4B;

Figure 4F is a digital representation of the graph of Figure 4D;

Figure 4G is a representation of the signal from the apparatus clock; and

Figure 5 is a graph of the first derivative of thoracic impedance as a function of time over a period of four heartbeats.

Description of the Preferred Embodiment

The invention may be used to monitor blood flow in any segment of tissue, however the following description refers to monitoring thoracic cardiovascular activity in order to provide a complete description of the new apparatus and method.

A continuous cardiac output monitor according to the invention uses an array of spot electrodes on the patient as shown in Figure 1. In a typical application, a pair of upper sensing electrodes 10 and 12 are attached to the patient's neck on opposite sides thereof at the intersections of the line encircling the root of the neck with the



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frontal plane. A pair of upper current injecting electrodes 14 and 16 are attached to the patient's neck approximately 3 to 5 centimeters above the upper sensing electrodes 10 and 12, respectively. A pair of lower thoracic anterior sensing electrodes 18 and 20 are placed at the intercostal space at each midclavicular line at the xiphoid process level. A pair of posterior sensing electrodes 22 and 24 shown in Figure 1B are placed at the same level as the anterior sensing electrodes 18 and 20 at the intercostal space at the midscapular line. Referring again to Figure 1A, a pair of lower current injecting electrodes 26 and 28 are located approximately 4 to 6 centimeters below the lower thoracic anterior sensing electrodes 18 and 20, respectively. Referring again to Figure 1B, a pair of lower injecting electrodes 30 and 32 are attached to the patient approximately 4 to 6 centimeters below the posterior sensing electrodes 22 and 24. All of the electrodes 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, and 32 are preferably spot electrodes which have been pregelled.

Referring to Figures 1A, 1B, and 2, a conductor 34 connects the upper injection electrodes to a current source 36, which preferably produces a high-frequency, constant amplitude current output. A conductor 38 connects both the anterior lower injection electrodes 26 and 28 and the posterior lower injection electrodes 30 and 32 to the current source 36. The frequency of the output of the current source 36 should be high enough to preclude any interference with proper functioning of the electrical systems within the human body. In a preferred embodiment of the invention, the current source 36 outputs a signal having an effective value of approximately 2.5 mA and a frequency of 70 kHz.

A conductor 40 connects the upper sensing electrodes 10 and 12 to a detector circuit 42. A conductor 44 connects the lower thoracic anterior sensing electrodes 18



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and 20 and the posterior sensing electrodes 22 and 24 to the detector circuit 42.

A noninvasive continuous cardiac output monitor according to the invention utilizes a modified systolic upstroke equation

$$SV = \frac{V_{ept}}{Z_0} T (\Delta Z/sec)$$

to calculate the stroke volume. V_{ept} is the physical volume of electrically participating thoracic tissue in milliliters, and the other variables in the equation are the same as those defined in connection with Kubicek's systolic upstroke equation discussed hereinabove. The volume of electrically participating tissue is a function of the thoracic volume, which approximates that of a cylinder

$$V_{ept} = \frac{C^2 L}{4\pi K}$$

Where C is the thoracic circumference; L is the average of the lines L_a and L_p , shown in Figures 1A and 1B respectively and which are distances between the lines through the center of the upper sensing electrodes 10 and 12 and the lower sensing electrodes 18 and 20 and 22 and 24; and K is a ratio constant approximately in the range 2.6 to 2.8 for a typical C/L ratio of about 3 for which the equation reduces to

$$V_{ept} = \frac{L^3}{4.25}$$

Referring to Figure 3, the graph illustrates typical variations in thoracic impedance due to respiratory and cardiovascular activity as a function of time. The average of the thoracic impedance is Z_0 . The variation of thoracic impedance due to respiratory activity is ΔZ_{resp} ; and ΔZ indicates variations of Z due to cardiovascular



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activity. As the graph of Figure 3 indicates, ΔZ_{resp} is much greater than ΔZ while the frequency of ΔZ is about four times the frequency of Z_{resp} .

The output signal, of the detector circuit 42 represents the thoracic impedance as a function of time. The circuitry of Figure 2 processes the thoracic impedance signal to obtain values for use in the modified systolic upstroke equation to monitor cardiovascular activity on a continuous basis.

The suppression of the effects of ventilation is depicted in Figure 5. Figure 5 shows the actual waveform of the first derivative of the impedance signal, including the effects of ventilation, as the signal emerges from the output terminal of the differentiation 48 (Figure 2). The signal shown in Figure 5 is supplied to the analog to digital (A/D) converter of the microprocessor 54. The microprocessor 54 measures the maximum positive value of the dZ/dt waveform ($\Delta Z/\text{sec}$, Figure 4C) at the time T_1 (Figure 4F), provided to the microprocessor 54 from the digital image (Figure 4F) of the second derivative of the impedance signal (Figure 4E) for every heartbeat. Referring to Figure 5, the microprocessor 54 will determine in four consecutive heartbeats the following $\Delta Z/\text{sec}$ magnitudes:

$$\Delta Z/\text{sec}_{(1)}; \Delta Z/\text{sec}_{(2)}; \Delta Z/\text{sec}_{(3)}; \text{ and } \Delta Z/\text{sec}_{(4)}.$$

Applying the sliding arithmetic average of the last four heartbeats, the microprocessor 54 will calculate the average value of $\Delta Z/\text{sec}_{(\text{AVER})}$, which then enters the calculation of stroke volume.

$$\Delta Z/\text{sec}_{(\text{AVER})} = \frac{\Delta Z/\text{sec}_{(1)} + \Delta Z/\text{sec}_{(2)} + \Delta Z/\text{sec}_{(3)} + \Delta Z/\text{sec}_{(4)}}{4}.$$

A comparator 50 receives the signal dZ/dt output from the differentiator 48 and functions as a zero-crossing



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detector to provide a constant logic one output voltage when the signal dZ/dt is positive and a logic zero output when the signal dZ/dt is negative. Thus, the comparator 50 produces in response to dZ/dt a digital signal which is high when dZ/dt is positive and low when dZ/dt is negative. Figure 4D is a graph of the digital representation of dZ/dt .

The clock for the apparatus is determined in the clock circuit 52, the output of which is shown in Figure 4G, and which is obtained in the digital form from the dZ/dt waveform (Figure 4C) when the waveform crosses the positive D.C. threshold.

Referring to Figures 2 and 4A, an electrocardiogram signal indicates the initiation of the systolic portion of a heartbeat, which determines the zero reference point for the time lines in Figures 4A - 4F.

Referring to Figure 4C, the ventricular ejection time T used in the calculation of the cardiac output is the time between the beginning of systolic contraction (time T_0) to the closure of the aortic valve (time T_2). The Time T_2 corresponds to the first negative minimum of dZ/dt waveform.

Obviously, the functions of the differentiator 48, the comparator 50, the clock 52, the differentiator 56, and the comparator 58 could be performed by software within the microprocessor 54.

A second differentiator 56 receives the output of the differentiator 48 and produces an output signal, shown in Figure 4E, which represents the second derivative, d^2Z/dt^2 , of the pulsatile thoracic impedance. A comparator 58 connected to the differentiator 56 digitizes d^2Z/dt^2 in a manner similar to that in which the comparator 50 digitizes the dZ/dt signal. The output of the comparator 58 is a digital signal which is high when d^2Z/dt^2 is positive and low when d^2Z/dt^2 is negative.

The digital representation of the second derivative of



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the pulsatile thoracic impedance function is shown in Figure 4F. The modified systolic upstroke equation used to calculate cardiac output utilizes the maximum value of the first derivative of the pulsatile impedance signal to calculate the stroke volume for each heartbeat. As shown in Figure 4C, the absolute maximum value of the first derivative of the pulsatile thoracic impedance is the first maximum which occurs after initiation of the systolic portion of the heartbeat. Referring to Figure 4E, the second derivative of the pulsatile thoracic impedance has a negative-going zero-crossing at the time at which the first derivative exhibits the absolute maximum value. In Figure 4F, the first negative-going pulse edge in the digital representation of the second derivative of the pulsatile thoracic impedance occurs at the time at which the first derivative of the pulsatile thoracic impedance exhibits the maximum value. Therefore, the microprocessor is programmed to read the value of the first derivative of the pulsatile thoracic impedance at the occurrence of the first negative-going pulse edge after initiation of the systolic portion of each heartbeat.

Thus, the signals input to the microprocessor 54 are the thoracic impedance from the detector circuit 42; the first derivative of the pulsatile thoracic impedance from the differentiator 48; the time interval between the first two positive going zero-crossings of the first derivative of the pulsatile thoracic impedance, which is the ventricular ejection time, from the comparator 50; and the digital representation of the second derivative of the pulsatile thoracic impedance. The microprocessor 54 has included therein analog to digital converters to enable the microprocessor 54 to process the analog signals from the detector circuit 42 and the differentiator 48. A thumb wheel switch 60 permits entry of the value of L needed to determine the volume of the electrically participating tissue. A display 62, which may be a



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digital readout display or a digital printer, provides means for an operator to read values of the various cardiac output parameters for which the microprocessor is programmed to compute. Typical values for cardiac parameters output by the display 62 are $Z_0 = 31$ ohms, $T = 0.39$ sec, $\Delta Z/\text{sec} = 0.99$ ohm/sec, $SV = 74$ ml, heart rate, $HR = 69/\text{min}$. and cardiac output = 5.1 liters/min.

Although the invention is described with reference to a specific preferred embodiment, modifications within the scope of the invention may be apparent to those skilled in the art. Therefore, the true scope of the invention is understood to be determined by the appended claims.



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WHAT IS CLAIMED IS:

1. Noninvasive apparatus for continuously monitoring cardiac output of a patient during normal respiratory functions, comprising:

5 means (42) for producing an electrical signal indicative of thoracic impedance as a function of time;

means (48) for eliminating effects of respiration from the thoracic impedance signal to produce a pulsatile impedance signal indicative of rate of changes in thoracic impedance due to cardiovascular activity as a function of time;

10 means (56) for processing the pulsatile rate of impedance change signal to produce a signal indicative of the maximum rate of change thereof as a function of time;

means (50) for processing the pulsatile impedance signal to produce a signal indicative of ventricular ejection time; and

20 computing means (54), responsive to the ventricular ejection time signal and to the maximum rate of change of pulsatile impedance signal, for producing a signal indicative of stroke volume.

2. The apparatus defined in Claim 1, additionally comprising:

25 means (52) for determining the heart rate; and computing means (54) for determining from said stroke volume and said heart rate, cardiac output.

3. Apparatus according to Claim 1 includes means (54) for averaging the maximum rate of the thoracic impedance change over a predetermined number of heartbeats of the patient.

4. Apparatus according to Claim 1, 2 or 3 wherein said means for producing an electrical signal indicative of thoracic impedance comprises:

35 a current source (36) having a high-frequency



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constant amplitude electrical current output;

injector electrodes (14, 16, 26, 28) for injecting the output of said current source into the thorax of the patient, said injector electrodes including a plurality of spot electrodes; and

sensor electrodes (10, 12, 18, 20) for sensing electrical current flow through the thorax of the patient, said sensor electrodes including an array of spot electrodes.

5. Apparatus according to Claim 1, 2 or 3 wherein said means for processing the pulsatile impedance signal to produce the signal indicative of the maximum rate of change of the pulsatile impedance signal includes:

first differentiator circuit (48) for producing a signal indicative of the first derivative of the pulsatile impedance signal;

second differentiator circuit (56), connected to the output of said first differentiator circuit (48), for producing a signal indicative of the second derivative of the pulsatile impedance signal; and

comparator means (58) for producing an output indicative of the zero-crossings of the signal indicative of the second derivative of the pulsatile impedance signal to indicate the maximum value of the first derivative of the pulsatile impedance signal after initiation of a heart beat.

6. Apparatus according to Claim 5 wherein said means for processing the pulsatile impedance signal to produce the ventricular ejection time signal includes:

second comparator (50), connected to said first differentiator circuit (48), for producing an output indicative of the zero-crossings of the first derivative of the pulsatile impedance signal; and

clock (52) for measuring the time interval between two consecutive heartbeats to determine heart rate.



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7. Apparatus according to Claim 1, 2 or 3 further including:

first differentiator circuit (48) for producing a signal indicative of the first derivative of the pulsatile impedance signal;

5

means (50) for producing a first digital logic signal responsive to the first derivative of the pulsatile impedance signal wherein a logic high represents positive values of the first derivative of the pulsatile impedance signal and a logic low represents negative values of the first derivative of the pulsatile impedance signal;

10

second differentiator circuit (56) connected to the output of said first differentiator circuit means for producing a signal indicative of the second derivative of the pulsatile impedance signal;

15

means (58) for producing a second digital logic signal responsive to the second derivative of the pulsatile impedance signal wherein a logic high represents positive values of the second derivative of the pulsatile impedance signal and a logic low represents negative values of the second derivative of the pulsatile impedance signal; and

20

means (54) for determining the value of the first derivative of the pulsatile impedance signal at the first negative-going pulse edge in the second digital logic signal after initiation of a heartbeat.

25

8. Apparatus according to Claim 7 further including:

means (54) for measuring the time interval between the first positive going zero-crossing in the first derivative digital logic signal and the first positive going zero-crossing in the second derivative logic signal after initiation of a heartbeat.

30

9. A noninvasive method for continuously monitoring cardiac output of a patient during normal respiratory functions, comprising the steps of:

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producing an electrical signal indicative of the thoracic impedance of the patient as a function of time;

5 eliminating the effects of respiration from the thoracic impedance signal, thereby producing a pulsatile impedance signal indicative of changes in thoracic impedance due to cardiovascular activity as a function of time;

10 processing the pulsatile impedance signal to produce a signal indicative of the maximum rate of change thereof;

processing the pulsatile impedance signal to produce a signal indicative of ventricular ejection time; and

15 computing a signal indicative of cardiac output as a function of the maximum rate of change of the pulsatile impedance signal and as a function of the maximum rate of change of the pulsatile impedance signal.

20 10. A method according to Claim 9 wherein producing an electrical signal indicative of thoracic impedance as a function of time further includes the steps of:

producing a high-frequency, constant amplitude electrical current;

25 injecting the high-frequency, constant amplitude electrical current into the thorax of the patient; and

sensing electrical current flow through the thorax of the patient.

30 11. A method according to Claim 9 wherein the step of processing the pulsatile impedance signal to produce a signal indicative of the maximum rate of change of the pulsatile impedance signal includes the steps of:

35 differentiating the pulsatile impedance signal to produce a signal indicative of the first derivative thereof;

differentiating the signal indicative of the



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first derivative of the pulsatile impedance signal to produce a signal indicative of the second derivative thereof; and

5 producing a signal indicative of the zero-crossings of the signal indicative of the second derivative of the pulsatile impedance signal to indicate the time of occurrence of the first maximum value and first minimum value of the first derivative of the pulsatile impedance signal occurring after
10 initiation of the systolic portion of a heartbeat.

12. A method according to Claim 11 wherein the step for processing the pulsatile impedance signal to produce the ventricular ejection time signal includes the steps of:

15 producing an output signal indicative of the zero-crossings of the first derivative of the pulsatile impedance signal; and

measuring the time interval between the first positive going zero-crossing of the first derivative of the pulsatile impedance signal and the first
20 positive going zero-crossing of the second derivative of the pulsatile impedance signal after initiation of the systolic portion of a heartbeat.

13. A method according to Claim 10, further including
25 the steps of:

producing a signal indicative of the first derivative of the pulsatile impedance signal;

producing a first digital logic signal responsive to the first derivative of the pulsatile impedance
30 signal;

producing a signal indicative of the second derivative of the pulsatile impedance signal;

producing a second digital logic signal responsive to the second derivative of the pulsatile
35 impedance signal; and

determining the value of the first derivative of



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the pulsatile impedance signal at the first negative-going pulse edge in the second digital logic signal after initiation of the systolic portion of a heartbeat.

5 14. A method according to Claim 13 further including
the step of measuring the time interval between the first
positive going zero-crossing in the first digital logic
signal and the first positive going zero-crossing of the
10 second digital logic signal after initiation of the
systolic portion of a heartbeat to determine the
ventricular ejection time.

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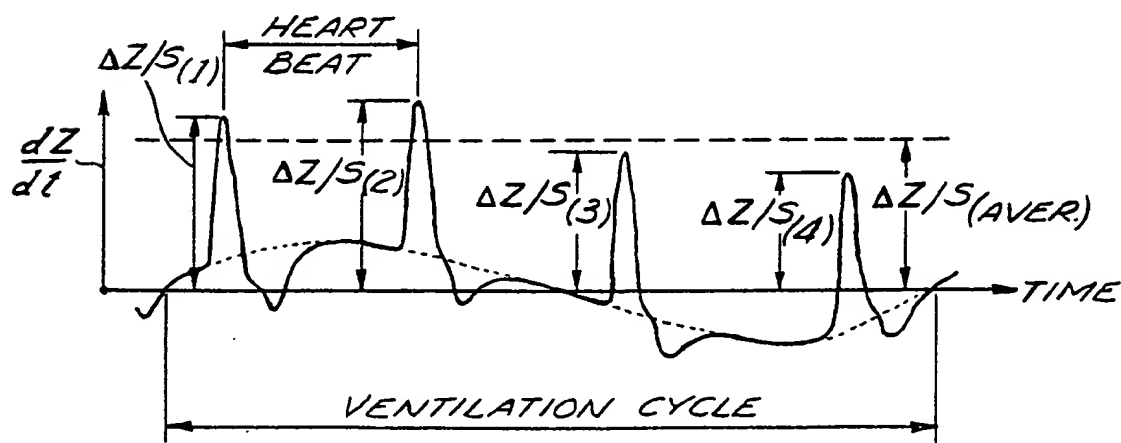
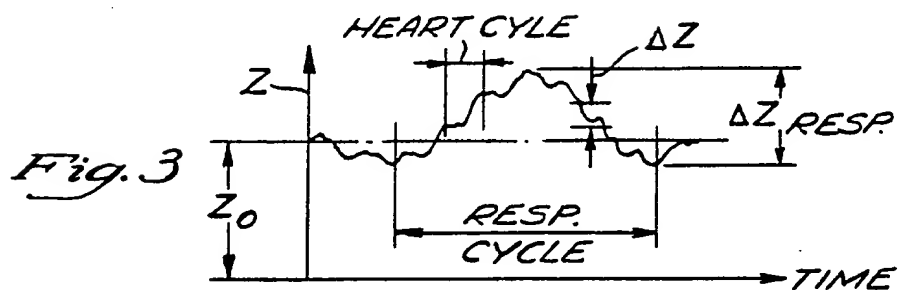
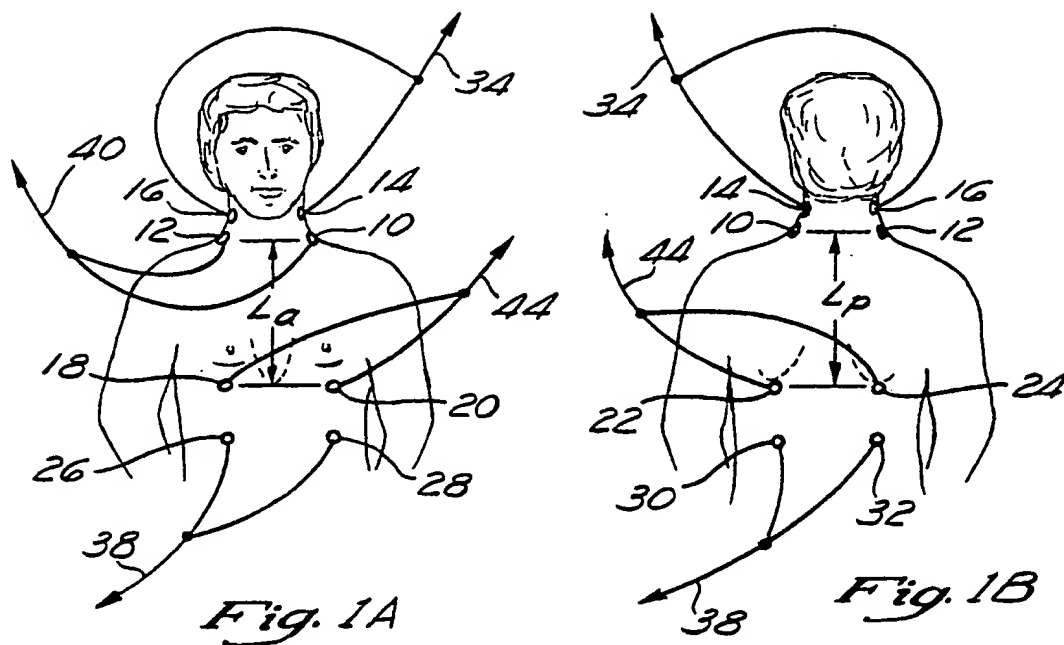


Fig. 5

SUBSTITUTE SHEET



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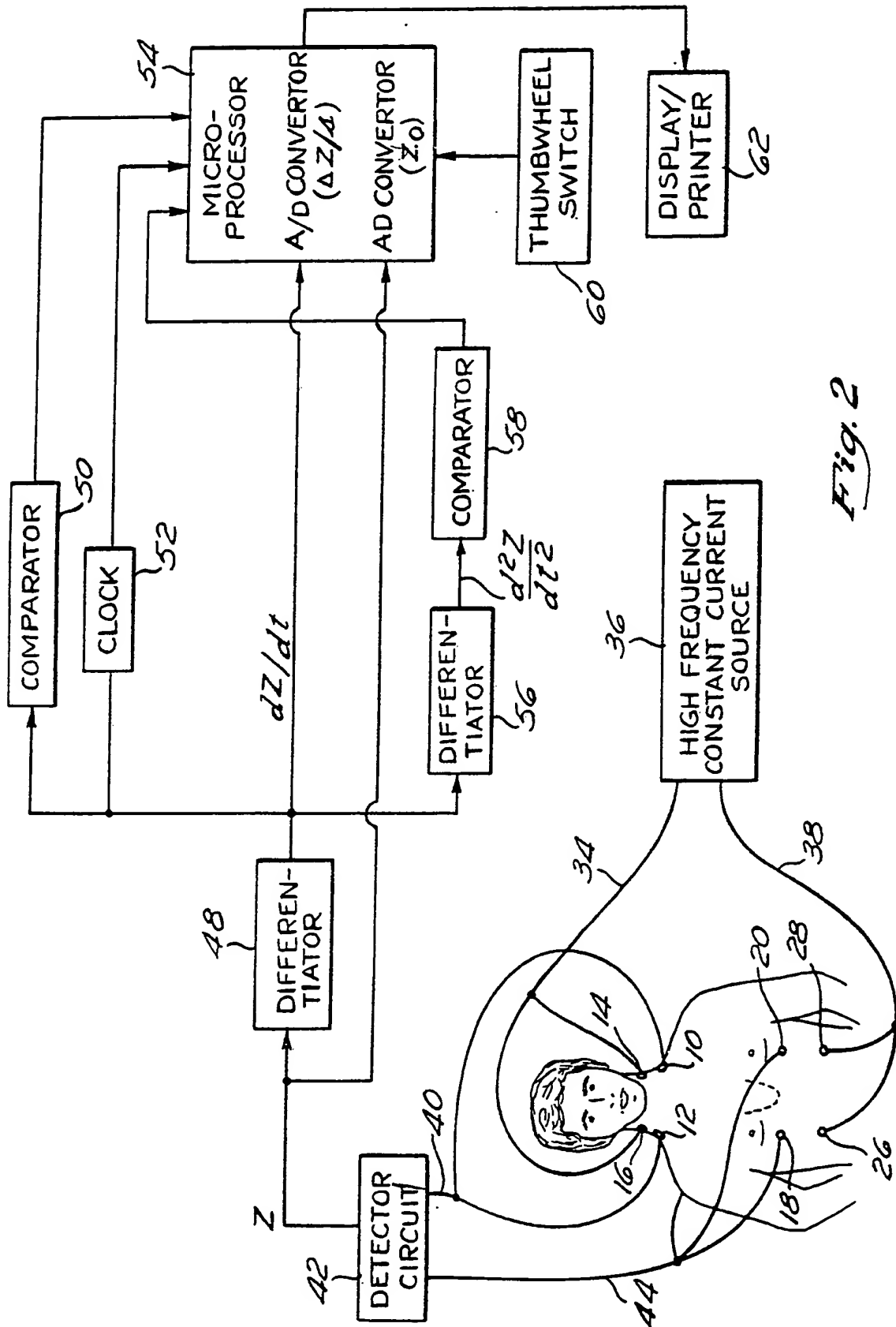


Fig. 2

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Fig. 4A

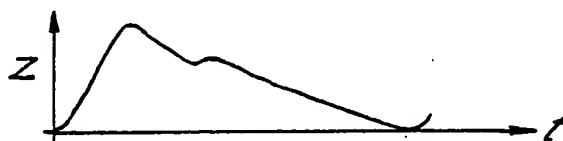


Fig. 4B

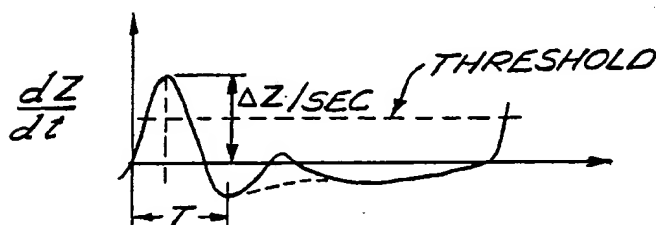


Fig. 4C

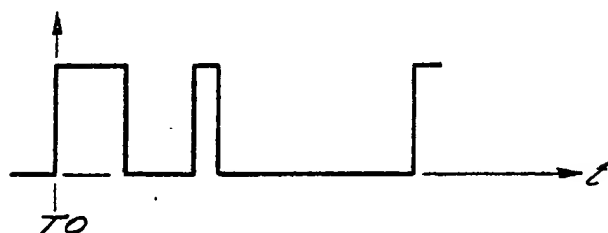


Fig. 4D

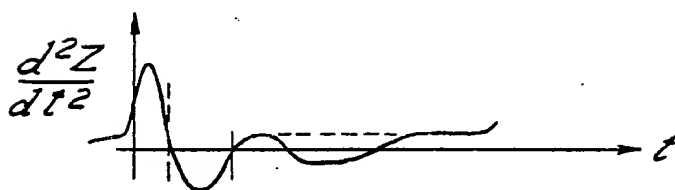


Fig. 4E

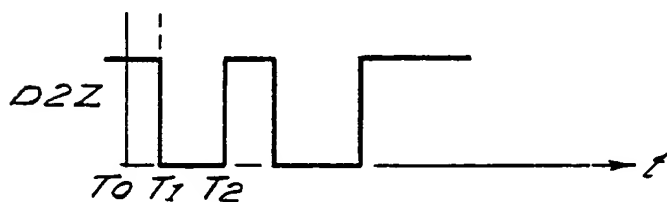


Fig. 4F



Fig. 4G

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US83/00987

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all) ¹ According to International Patent Classification (IPC) or to both National Classification and IPC <div style="display: flex; justify-content: space-between; font-family: monospace;"> INT. CL.⁹ G06F 15/42, H03K 13/02, A61B 5/02, A61B 5/04 U.S. CL. 364/415, 416 128/693, 670, 720, 734 A61B 5/05 </div>																										
II. FIELDS SEARCHED <div style="text-align: center; font-size: small;">Minimum Documentation Searched ⁴</div> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <th style="width: 20%; text-align: left;">Classification System</th> <th style="text-align: left;">Classification Symbols</th> </tr> <tr> <td style="vertical-align: top;">U.S.</td> <td>128/693, 694, 670, 671, 720, 725, 734 364/415, 416, 417</td> </tr> </table> <div style="text-align: center; font-size: x-small; margin-top: 5px;">Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁵</div>			Classification System	Classification Symbols	U.S.	128/693, 694, 670, 671, 720, 725, 734 364/415, 416, 417																				
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III. DOCUMENTS CONSIDERED TO BE RELEVANT ¹⁴ <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <th style="width: 5%; text-align: left;">Category ⁶</th> <th style="width: 70%; text-align: left;">Citation of Document, ¹⁰ with indication, where appropriate, of the relevant passages ¹⁷</th> <th style="width: 25%; text-align: left;">Relevant to Claim No. ¹⁸</th> </tr> <tr> <td style="vertical-align: top;">A</td> <td>US,A, 3,730,171 (Namon) 01 May 1973</td> <td>1-14</td> </tr> <tr> <td style="vertical-align: top;">A</td> <td>US,A, 3,835,840 (Mount) 17 September 1974</td> <td>1-14</td> </tr> <tr> <td style="vertical-align: top;">A</td> <td>US,A, 3,835,839 (Brown) 17 September 1974</td> <td>1-14</td> </tr> <tr> <td style="vertical-align: top;">A</td> <td>US,A, 3,871,359 (Pacela) 18 March 1975</td> <td>1-14</td> </tr> <tr> <td style="vertical-align: top;">A</td> <td>US,A, 3,882,851 (Sigworth) 13 May 1975</td> <td>1-14</td> </tr> <tr> <td style="vertical-align: top;">A</td> <td>US,A, 3,994,284 (Voelker) 30 November 1976</td> <td>1-14</td> </tr> <tr> <td style="vertical-align: top;">A</td> <td>US,A, 3,996,925 (Djordjevich) 14 December 1976</td> <td>1-14</td> </tr> </table> <div style="font-size: x-small; margin-top: 10px;"> <div style="display: flex; justify-content: space-between;"> <div style="width: 48%;"> <p>[*] Special categories of cited documents: ¹⁵</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 48%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</p> <p>"&" document member of the same patent family</p> </div> </div> </div>			Category ⁶	Citation of Document, ¹⁰ with indication, where appropriate, of the relevant passages ¹⁷	Relevant to Claim No. ¹⁸	A	US,A, 3,730,171 (Namon) 01 May 1973	1-14	A	US,A, 3,835,840 (Mount) 17 September 1974	1-14	A	US,A, 3,835,839 (Brown) 17 September 1974	1-14	A	US,A, 3,871,359 (Pacela) 18 March 1975	1-14	A	US,A, 3,882,851 (Sigworth) 13 May 1975	1-14	A	US,A, 3,994,284 (Voelker) 30 November 1976	1-14	A	US,A, 3,996,925 (Djordjevich) 14 December 1976	1-14
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IV. CERTIFICATION <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%; vertical-align: top;"> Date of the Actual Completion of the International Search ¹ <div style="text-align: center; font-size: large;">16 AUGUST 1983</div> </td> <td style="width: 50%; vertical-align: top;"> Date of Mailing of this International Search Report ³ <div style="text-align: center; font-size: large;">15 SEP 1983</div> </td> </tr> <tr> <td style="vertical-align: top;"> International Searching Authority ¹ <div style="text-align: center; font-size: large;">ISA/US</div> </td> <td style="vertical-align: top;"> Signature of Authorized Officer ¹⁰ <div style="text-align: center;"> </div> </td> </tr> </table>			Date of the Actual Completion of the International Search ¹ <div style="text-align: center; font-size: large;">16 AUGUST 1983</div>	Date of Mailing of this International Search Report ³ <div style="text-align: center; font-size: large;">15 SEP 1983</div>	International Searching Authority ¹ <div style="text-align: center; font-size: large;">ISA/US</div>	Signature of Authorized Officer ¹⁰ <div style="text-align: center;"> </div>																				
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A

US,A, RE. 30,101 (Kubicek et al)
25 September 1979

1-14

V. ☐ OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE ¹⁰

This international search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1. ☐ Claim numbers _____, because they relate to subject matter ¹² not required to be searched by this Authority, namely:

2. ☐ Claim numbers _____, because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out ¹³, specifically:

VI. ☐ OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING ¹¹

This International Searching Authority found multiple inventions in this international application as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.

2. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:

3. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:

4. ☐ As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

☐ The additional search fees were accompanied by applicant's protest.

☐ No protest accompanied the payment of additional search fees.